IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Appln. Ser. No.:	Filed:	Inventor(s):	Atty Dkt:
09/576,597	22 May 2000	J. J. Voorhees *et al.*	100UM-009A

Title: Compositions and Methods for Use Against Acne-induced Inflammation and Dermal Matrix Degrading Enzymes

Examiner: Vicky Y. Kim	Art Unit: 1614

Asst. Comm'r for Patents
Washington, D.C. 20231-0001

Declaration Under 37 C.F.R. § 1.132 by Dr. Fisher

Dear Sir:

In connection with the above-identified application, I declare as follows:

1. My name is Gary J. Fisher. I am a named co-inventor of this patent application. Presently, I hold the position of Associate Professor, Department of Dermatology, at the University of Michigan. I earned my Ph.D. in Biochemisty from Cornell University in 1980. I have worked as a consultant in the pharmaceutical industry for almost twelve years, and I have been active in research in the field of dermatology for over 17 years. A copy of my *curriculum vitae* is attached.

2. I have read and understood the subject patent application, as well as the office action mailed December 5, 2003, and the Pikul *et al.* patent cited by the examiner. It is my understanding that the examiner's position is that

Pikul teaches using MMP inhibitors to prevent acne scarring. I respectfully disagree.

3.a. Pikul is directed to a genus of compounds that are stated in the patent to be phosphinic acid amide matrix metalloproteinase ("PAAMMP") inhibitors.

3.b. As one having worked in the field of biochemistry for over twenty years, and almost that long studying physiological effects, I would have expected Pikul to provide some sort of objective, *in vitro*, evidence of actual inhibition of MMP activity. Pikul describes that assays exist for testing the specificity of MMP inhibitors. Column ten, lines 43-59. Because testing for actual inhibition of MMP activity is relatively simple, I would have expected Pikul to provide some results from such assays, but I could not find any such results in the patent publication.

3.c. The attached article by Whittaker *et al.* (*Chem. Rev.* 1999, *99*, 2735-2776) is a review of structurally and mechanistically different MMP inhibitors, and provides specificity and structural data for some. Taking any specific compound at random, the Whittaker data shows that specificity is variable, though the article gives structural approaches for altering or improving specificity. One of the compounds disclosed by Whittaker as compound 66 is described as a hydroxamide having come from the Pikul group (p. 2757).

3.d. The attached article by Vassiliou *et al.* (*J. Med. Chem.* **1999**, *42*, 2610-2620) describes phosphinic amide pseudo-tripeptide MMP inhibitors,

although none have a nitrogen bonded to a phosphorous as in Pikul. These compounds are "highly potent" MMP inhibitors provided they contain "an unusual long aryl–alkyl substituent" at a particular position in the molecule.

3.e. The attached article by Reiter *et al.* (*Bioorg. & Med. Chem. Letters* 13 (2003) 2331-2336) discloses phosphinic amide inhibitors that are selective for MMP-13, although none have a nitrogen bonded to a phosphorous as in Pikul.

3.f. Whittaker, Vassiliou, and Reiter all disclose some sort of data, and a methodology, by which I can understand that certain compounds, at least the compounds for which data is provided, are likely to have biological activity because of particular *in vitro* data. In my opinion, the Pikul patent provides no data that would be suggestive of biological activity for any of the compounds disclosed. My opinion is bolstered by the fact that all of the examples, both the syntheses and the preparation of dosage forms, are written in the present tense, indicating they are prophetic, so that no experiment, synthesis, or preparation was actually conducted.

4.a. The Pikul patent goes to some length in discussing various medical conditions for which matrix metalloproteinase inhibitors have a "potential" therapeutic use. It has been known since well before the Pikul patent that there are many types of collagen as well as many types of MMPs (there are presently some 23 different types of MMPs).

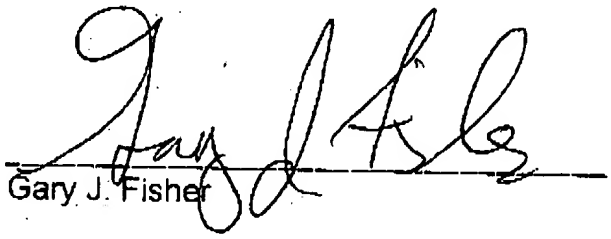
4.b. Not discussed by Pikul is that different MMPs have been implicated in different medical conditions. One must know which MMP(s) to inhibit to treat a given condition.

4.c. To my knowledge, ours was the first group to discover that MMP-1 and MMP-8 are active in acne lesions. Our patent application includes *in vivo* data obtained from human volunteers substantiating this discovery.

4.d. Because Pikul gives no indication which MMP(s) to inhibit in the treatment of acne, nor which of his compounds is selective for that MMP inhibitor(s) (nor which of his compounds actually inhibits any MMP), it is my opinion that Pikul's disclosure does not teach any connection between acne scarring and MMP inhibition, and is specifically deficient with respect to inhibiting MMP-1 or MMP-8 in the treatment of acne scarring.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issued thereon.

Date: 5/12/04



Gary J. Fisher

CURRICULUM VITAE

PERSONAL DATA

Name:	Gary J. Fisher
Employee ID:	0535 2372

EDUCATION

1969-1974	University of California San Diego, BA (Biology).
1974-1980	Cornell University, Ph.D. (Biochemistry)

POSTDOCTORAL TRAINING

1980-1983	Washington University, Biological Chemistry

ACADEMIC APPOINTMENTS

1985-1989	Research Investigator, Department of Dermatology, University of Michigan
1989- 1994	Assistant Research Scientist, Department of Dermatology, University of Michigan
1994-1997	Associate Research Scientist, Department of Dermatology, University of Michigan
1997-1999	Senior Associate Research Scientist, Department of Dermatology, University of Michigan
1999-present	Associate Professor, Department of Dermatology, University of Michigan

SENIOR POSTDOCTORAL TRAINING

1983-1985	Washington University, Laboratory Medicine

CONSULTING POSITIONS

1992- 1995	Schering-Plough
1995 - present	DuPont Merck

SCIENTIFIC ACTIVITIES

University of Michigan

1990-present	Comprehensive Cancer Center Member
1991-present	Laboratory Director "Molecular Mechanisms of Skin Repair" Department of Dermatology/Johnson & Johnson Research Alliance
2003-2004	Reviewer for Biomedical Research Grant Application
2003-2004	Reviewer for General Clinical Research Center

Editorial Board

1999-present	Associate Editor, Journal for Investigative Dermatology

SCIENTIFIC ACTIVITES {cont'd}

Reviewer

1988 - present	Archives of Dermatological Research
1988 - present	British Journal of Dermatology
1988 - present	Journal of Investigative Dermatology
1990 - present	Canadian Journal of Microbiology
1990 - present	Journal of Cellular Physiology
1990 - present	Journal of Dermatological Science
1991 - present	Lipid Research
1992 - present	Molecular Pharmacology
1996 - present	Nature Medicine
1996 - present	Journal of Clinical Investigation
1997 - present	Journal of Photochemistry and Photobiology
2000-	Society for Investigative Dermatology Committee on Scientific Programs

Study Sections

1991	NIH, Site Visit
1992	NIH, Ad Hoc Member
1996-2000	NIH, Reviewers Reserve
2002-2004	American Heart Association National Center
2003	NIH, Reviewer Project Grant

Co-Chair

1990	Society for Investigative Dermatology
1995	Society for Investigative Dermatology
1996	Society for Investigative Dermatology
1997	Society for Investigative Dermatology
2000	Society for Investigative Dermatology
2001	Society for Investigative Dermatology
2002	Society for Investigative Dermatology
2003	Society for Investigative Dermatology
2004	Society for Investigative Dermatology

GRANT SUPPORT

Dermatology Foundation
Project Director
"Molecular Mechanisms of Retinoids on Human Epidermis"
01/01/88 - 12/31/88 ($10,000 annual direct costs)

Dermatology Foundation
Project Director
"Activation of Phospholipase C in Human Keratinocytes"
01/01/89 - 12/31/89 ($25,000 annual direct costs)

Dermatology Foundation
Project Director
"Role of PLC/PKC Signal Transduction System in Keratinocytes"
01/01/90 - 12/31/90 ($25,000 annual direct costs)

GRANT SUPPORT
(cont'd)

Dermatology Foundation
Project Director
"Role of Retinoic Acid Receptors in Human Skin"
01/01/90 - 12/31/90 ($25,000 annual direct costs)

Dermatology Foundation
Project Director
"Role of Retinoid Binding Proteins and Receptors in Human Skin Gene Regulation"
01/01/91 - 12/31/91 ($25,000 annual direct costs)

Dermatology Foundation
Project Director
"Functional Specificities of Protein Kinase C Isozymes in Human Keratinocytes"
01/01/92 - 12/31/93 ($25,000 annual direct costs)

Lester Conrad
Principal Investigator
"Mechanism of Cutaneous Photoaging: Synthesis and Degradation of Type I and III Collagen in Chronically Sun-exposed Human Skin"
12/01/92 - 11/30/93 ($10,000 annual direct costs)

National Institutes of Health
Principal Investigator
(R29-AR39691) "Phospholipase C / Protein Kinase C in Psoriatic Epidermis"
04/01/89 - 03/31/94 (approximately $70,000 annual direct costs)

Dermatology Foundation
Project Director
"Role and Regulation of Cellular Retinoic Acid Binding Proteins (CRABPs) and CRABP Genes in Human Skin"
01/01/92 - 12/31/94 ($40,000 annual direct costs)

Dermatology Foundation
Project Director
"Mechanisms of Transcriptional Regulation of Retinoid-Responsive Genes by Retinoic Acid and Retinoid X Receptors in Human Keratinocytes"
01/01/94 - 12-31-94 ($25,000 annual direct costs)

Unilever
Co-Investigator
"Cell and Molecular Response of Normal Human Skin to External Stimuli"
Subgrant: "Signal Transduction"
01/01/93 - 12/31/96 ($82,000 annual direct costs)

GRANT SUPPORT (cont'd)

National Institute of Health
Principal Investigator
(R01) "Function of Protein Kinase C Isoenzymes in Human Keratinocytes"
08/01/95 - 07/31/98 ($547,805 direct costs)

Dermatology Foundation
Principal Investigator
"Mechanisms of ubiquitin proteasome-mediated degradation of retinoid and vitamin D receptors in human skin and cultured keratinocytes"
7/1/99 to 6/30/00($10,000 direct costs)

Johnson & Johnson
Director of Laboratory Research/Co-Investigator
"Molecular Mechanisms of Skin Aging and Repair "
01/01/91 - 1/31/03 ($877,684 annual direct costs)

Current:

National Institutes of Health Training Grant
Co-Investigator
(5T32AM07197-16) "Training Grant in Cell and Molecular Dermatology"
07/01/92 - 06/30/01 (approximately $90,648 annual direct costs)

National Institute of Health
Principal Investigator
"TGF-β signaling in photoaged and chronologically aged human skin"
02/01/02 – 01/31/07 (377,500 annual costs)

Pfizer, Inc.
Principal Investigator
"Pharmacological Modulation of Skin Collagen"

Pending

National Institute of Health
Principal Investigator
"Receptor Protein Tyrosine Phosphatase Regulation of EGFR"

National Institute of Health
Principal Investigator
"Stem Cells in Aging Human Skin *in vivo*"

National Institute of Health
Principal Investigator
"Collagenase Degradation of Extracellular Matrix in Aging"

HONORS AND AWARDS

1974 University of California Presidents Research Award
2001 University of Michigan Inventor Recognition Award
2001 University of Michigan Medical School Dean's Award for Achievement in Clinical and Basic Science Research

MEMBERSHIPS AND OFFICES IN PROFESSIONAL SOCIETIES

1998-present	Society for Photobiology
1993-present	American Association for the Advancement of Science
1986-present	American Society for Biochemistry and Molecular Biology
1986-present	Society for Investigative Dermatology
1990-1992	Skin Pharmacology

TEACHING ACTIVITIES

University of Michigan

Departmental Seminars

2000-present	Basic Science Journal Club with Clinical Residents {5 hours per month}
1986-present	Critical Analysis of Journal and Scientific Issues with Research Fellows {1.5 hours per week}
1990- present	Dermatology Research Conference {2 hours per month}

Member of Training Program

1992-2003	National Institutes of Health Training Grant "Training Grant in Cell and Molecular Dermatology"

Dissertation Committee

1994	MD Dissertation - NJ Reynolds
2003	PhD Thesis Committee for Tsu Wei

Invited Teaching Presentations

1994	Graduate Seminar in Pharmacology
1994	Graduate Seminar in Biochemistry
1998	Graduate Seminar in Physiology
1999	Graduate Seminar in Organogenesis of the Skin
2000	Dermatology Sesquicentennial Grand Rounds
2001	Seminar in Nephrology

Mentoring

Directed research training within a multi-faceted laboratory setting for the following research fellows, dermatology residents, and beginning faculty.

JT Elder, MD, PhD
AK Gupta, MD
H Takematsu, MD
N Ryder, PhD
J Esmann, MD
CEM Griffiths, MD
QY Zhang, PhD
H Talwar, PhD
ZQ Wang, PhD
Yiru Xu, PhD
Shin Murakami, PhD
NJ Reynolds, MD
JL Shuler, PhD
SB Kurlandsky, PhD
JY Yi, MD
FG Larsen, MD
JH Choi, MD
A Tuschill, PhD
PP Lin, PhD
C Zoboulis, M.D.
F McPhillips, PhD
Y Marikar, PhD
A Asuru, PhD
ZQ Wang, PhD
A Belt, PhD
JH Chung, MD
H Choi, MD
JH Lee, MD
YS Wan, PhD
M Boudjelal, PhD
TY He, PhD
V Roxas, PhD
Y Shao, PhD
G Pugh, PhD
TH Quan, PhD
G Xu, Ph.D.
L Tan, Ph.D.
HQ Wang, PhD
L Ritté, PhD
Lin Lin, PhD

University of Michigan Department of Dermatology
Mentoring of Junior Faculty

Anders Astrom, PhD	Steven Madore, PhD	Knud Kragballe, M.D., Ph.D.
Amir Tavakkol, PhD	JiaHao Xiao, PhD	Yiru Xu, Ph.D.
Ambati Reddy, PhD	XiaoYan Li, PhD	Taihao Quan, M.D., Ph.D.
Harvinder Talwar, PhD	ZenqQuan Wang, PhD	Shin Murakami, Ph.D.
Jiayuh Lin, PhD	Subhash Datta, PhD	

EXTRAMURAL INVITED PRESENTATIONS

International

"Topical retinoic acid increases transforming growth factor-beta 1 immunoreactivity but not its mRNA in human epidermis *in vivo*", International Investigative Dermatology, Washington DC, 1990.

"Quantitation of endogenous nuclear retinoid receptor proteins in human epidermis *in vivo*: High levels of retinoic acid receptor gamma and retinoid X receptor alpha that bind to a retinoic acid response element exclusively as heterodimers", International Investigative Dermatology, Japan, 1994.

"UVB Activates Stress-Activated Protein Kinases, fos/jun and fos/jun Driven Dermis-Degrading Proteinases in Human Skin *in vivo*", European Society for Dermatological Research, Amsterdam, 1996.

"The transcription factor c-jun is critical for ultraviolet irradiation-induced premature aging and its prevention by retinoic acid in human skin *in vivo;"* European Society for Dermatological Research, Italy, 1997.

"Ultraviolet irradiation rapidly activates cell surface receptors and three distinct MAP kinase modules in human skin *in vivo*", Society for Investigative Dermatology, Cologne Germany, 1998.

"UV Signal Transduction in Human Skin", Korean Dermatological Association, Seoul Korea, April 26, 2000.

" UV Signaling in Human Skin", Seoul University, April 28, 2000

"UV-Induced Cell Signalling Pathway", International Workshop on Molecular Mechanisms of Tanning, Nice France, April 26-29, 2001.

"Regulation of UV-induced Signal Transduction by Receptor Protein Tyrosine Phosphatases in Human Skin", Southampton England, GlaxoSmithKline Guest Speaker, British Society for Investigative Dermatology, April 7-9, 2003.

"Ultraviolet Irradiation Activates NF-κβ Pathway via Association of IκB Kinase-γ/NEMO with IκB kinase-β and IκB-α in Human Keratinocytes". International Investigative Dermatology, April 30-May 4, 2003.

"UV-induced Signaling Pathway that Mediate Photoaging in Human Skin", 14th International Congress on Photobiology, Jeju Korea, June 10-14, 2004.

National

"Protein kinase C regulates terminal differentiation in cultured adult human keratinocytes", Society for Investigative Dermatology, Washington, D.C., 1988.

"Protein kinase C isoforms alpha and beta are expressed in adult human epidermis", Society for Investigative Dermatology, Washington D.C., 1989.

"Genes for the calcium independent protein kinase C isoforms delta, epsilon, & L are expressed in human epidermis and cultured keratinocytes", Society for Investigative Dermatology, Seattle, Washington, 1991.

"Differential expression of conventional and nonconventional protein kinase C isozymes in normal and psoriatic skin", Society for Investigative Dermatology, 1992.

"Protein kinase C isoenzymes alpha and epsilon are translocated and down-regulated by phorbol ester and bryostatin-1 in human keratinocytes and fibroblasts", Society for Investigative Dermatology, 1993.

"Ultraviolet irradiation rapidly upregulates transcription factors AP-1 and NF-κB and subsequently induces expression of target genes for matrix-degrading metalloproteinases in human skin *in vivo*", Society for Investigative Dermatology, 1995.

"Retinoic acid antagonizes UVB activation of AP-1 and inhibits induction of matrix metalloproteinases in human epidermis and dermis *in vivo*", Society for Investigative Dermatology, 1996.

"Ultraviolet irradiation damages the dermis by both degrading collagen and inhibiting procollagen synthesis: Protection by all-*trans* retinoic acid in human skin *in vivo*", Society for Investigative Dermatology, 1997.

"Overview of Growth Factors and Signal Transduction", Society for Investigative Dermatology, Chicago IL, 1999.

"Mechanisms of Photoaging", Parke-Davis Warner Lambert, June 7, 2000

"Retinoids in research and human skin", Galderma and Society for Investigative Dermatology, May 14-19, 2002.

"UV regulation of collagen in human skin", Scleroderma Workshop, Boston University, May 20-22, 2002.

"UV regulation of TGF-β signaling in human skin", University of Illinois at Chicago Rheumatology Grand Rounds, November 19-20, 2002.

"The Pathophysiology of Damaged Skin", Contemporary Perspectives on Topical Retinoids, Ameila Island FL, March 22, 2004.

"When does skin aging begin?", NIH Aging Workshop, Bethesda MD, May 5-7, 2004.

University of Michigan

"PKC isoenzymes expression and function in human skin", Graduate Seminar in Pharmacology, 1994.

"Matrix metalloproteinases as mediators of UV-induced skin damage", Graduate Seminar in Biochemistry, 1995.

"UV signaling pathways in human skin", Graduate Seminar in Physiology, 1998.

"Mechanisms of premature skin aging", Graduate Seminar in Organogenesis of the Skin, 1999.

"Retinoid signaling in human skin", Graduate Seminar in Organogenesis of the Skin, 1999.

"The mechanisms of Photoaging", U of Michigan Medical School Sesquicentennial, October 13, 2000.

"UV Signaling in human keratinocytes", St Louis University, March 20, 2001.

"UV signaling in human skin", Basic Science Seminar for Nephrology, U of Michigan, March 27, 2001.

OTHER PRESENTATIONS

International

"Protein kinase C in normal and psoriatic adult human epidermis", Recent Advances in Prostaglandin and Leukotriene Research Florence, Italy, 1987

"Cyclosporine A inhibits growth of human keratinocytes in serum free, but not serum containing media", International Conference on Mechanisms of Cyclosporine Action, Washington D.C., 1988.

"Properties and functions of protein kinase C in psoriasis", Sandoz Research Institute, Vienna, Austria, 1990.

"Expression and function of protein kinase C in psoriasis", International Psoriasis Meeting, San Francisco, California, 1991.

"Pharmacological, cellular and molecular aspects of topical retinoic acid treatment in humans", Retinoids 10 years On, Geneva, Switzerland, 1991.

"All-*trans* retinol mimics the biological effects of all-trans retinoic acid in human skin through metabolic conversion to all-trans retinoic acid", Retinoids 1995, Sophia Antipolis, France, 1995.

"Effect of All-trans-retinoic Acid on Aging Processes", FASEB Summer Conference, Snowmass, Colorado, 1996.

"Retinol Metabolism and actions in human skin", Retinoids '97, France, 1997.

"Molecular mechanisms of photoaging and its prevention by retinoic acid: ultraviolet irradiation induces MAP kinase signal transduction cascades that induce AP-1-regualted matrix metalloproteinases that degrade human skin *in vivo*", 46th Symposium on the Biology of Skin, Snowmass Colorado, 1997.

"Retinoic Acid Antagonism of AP-1 in UV-Irradiated Human Skin", FASEB Summer Conference, Snowmass, Colorado, 1997

"Retinoids", FASEB Summer Research Conference, Snowmass Colorado, June 13-18, 1998.

"Molecular Pathophysiology of Photoaging in Human Skin and the Effect of all-*trans* Retinoic Acid," Biologic Effects of Light Symposium, Basel, Switzerland, November 1-3, 1998.

National

"Role of protein kinase C in the pathophysiology of psoriasis", Sphinx Pharmaceuticals, Durham, North Carolina, 1990.

"Phosphoinositide mediated signal transduction in normal and psoriatic epidermis", Psoriasis Workshop, Park City, Utah, 1990.

"Role of the phospholipase c/protein kinase C signal transduction system in psoriasis", Schering-Plough, Bloomfield, New Jersey, 1991.

"Role of protein kinase C in regulation of cellular homeostasis in human skin", Collagen Corporation, Palo Alto, California, 1992.

"Role of the phospholipase c/protein kinase C signal transduction system in cutaneous inflammation", Hoffman LaRoche, Nutley, New Jersey, 1992.

"Properties and functions of protein kinase C isoenzymes in normal and psoriatic human skin", Keystone Symposium, Silverthorne, CO, 1994.

"The retinoid signaling pathway in human skin", St. Louis University, St. Louis, Missouri, 1995.

"Ultraviolet irradiation induced signal transduction leading to matrix metalloproteinase gene expression in human skin *in vivo*", American Society for Photobiology, St Louis MO, 1997.

"All-*trans* retinoid acid protects against increased collagen breakdown and reduced collagen synthesis caused by ultraviolet irradiation in human skin *in vivo*", American Society for Photobiology, Snowbird, Utah July 13-16, 1998.

"Photoaging Caused by Ultraviolet Irradiation in Human Skin *in vivo* Results in Increased Collagen Breakdown and Reduced Collagen Synthesis", NIAMS Research Workshop on Risks and Benefits of Exposure to Ultraviolet Radiation and Tanning, Washington DC September 16-18, 1998.

"UV Signaling in Human Skin," University of Texas Southwestern, Dallas TX January 25, 1999

"UV Signal Transduction and Human Skin Aging", State University of New York, Stony Brook, NY, March 18, 1999.

COMMITTEE AND ADMINISTRATIVE SERVICES

University of Michigan

1986-present	Department of Dermatology Internal Review Committee
1986-present	Department of Dermatology Resident Recruitment
1989-present	Department of Dermatology Faculty and Postdoctoral Recruitment Committee
1991-present	Department of Dermatology Laboratory Planning and Renovation Committee
1993-present	Department of Dermatology Faculty Promotions Committee
1998-present	Department Strategic Planning Committee
2001-present	Medical School Student Biomedical Research Program Faculty Mentor
2001-present	Office of Research & Graduate Studies and the Associate Chairs for Research

PATENTS

Methods of Inhibiting Photoaging of Skin, US Patent No. 5,837,224, November 17, 1998.

Improving Keratinocyte and Fibroblast Proliferation, Decreasing Matrix Metalloproteinase Expression, and Improving Collagen Synthesis in the Elderly, #60/040,594, pending.

Compositions and Methods for Inhibiting Photoaging of Skin, 60/048,520, pending.

Methods and Compositions for Reducing UV-Induced Inhibition of Collagen Synthesis in Human Skin, #60/080,437, pending

Retinol Inhibition of UV-Induced Inflammation in Human Skin, 60/108,911, pending.

Prevention of UV-Induction Functional Vitamin A Deficiency Through the Use of Topically Applied Retinoid, 09/418,413, pending.

Compositions and Methods for Using MMP Inhibitors Against Acne-Induced Degradation of Human Skin, pending.

Use of EGF-R Protein Tyrosine Kinase Inhibitors for Preventing Photoaging in Human Skin, pending.

BIBLIOGRAPHY

Completed Publications in Scientific Journals

Peer Reviewed Publications

1. Trzaskos JM, Bowen W, Fisher GJ, Billheimer JT, Gaylor JL: Microsomal enzymes of cholesterol biosynthesis from lanosterol. Lipids 17:250-256, 1981.
2. Fisher GJ, Fukushima H, Gaylor JL: Isolation, purification, and characterization of a unique form of cytochrome P-450 in microsomes of isosafrole-treated rats. J Biol Chem 256:4388-4394, 1981.
3. Fisher GJ, Gaylor JL: Kinetic investigation of rat liver microsomal electron transport from NADH to cytochrome P-450. J Biol Chem 257:7449-7455, 1981.
4. Fisher GJ, Freter CE, Ladenson RC, Silbert DF: Effect of membrane sterol content on the susceptibility of phospholipids to phospholipase A. J Biol Chem, 258:11705-11712, 1983.
5. Baldassare JJ, Bakshian S, Knipp MH, Fisher GJ: Inhibition of human platelet fibrinogen receptor expression and serotin release by leupeptin and antipain. J Biol Chem 260:10531-10535, 1985.
6. Fisher GJ, Bakshian S, Baldassare JJ: Activation of human platelets by ADP causes a rapid rise in cytosolic free calcium without hydrolysis of phosphatidylinositol-4,5-bisphosphate. Biochem Biophys Res Comm 129:958-964, 1985.
7. Baldassare JJ, Fisher GJ: GTP and cytosol stimulate phosphoinositide hydrolysis in isolated platelet membranes. Biochem Biophys Res Comm 137:801-805, 1986.
8. Horn F, Marks F, Fisher GJ, Marcelo CL, Voorhees JJ: Decreased protein kinase C in psoriatic versus normal epidermis. J Invest Dermatol 88:220-222, 1986.
9. Nickoloff BJ, Fisher GJ, Mitra RS, Voorhees JJ: Additive and synergistic antiproliferative effects of cyclosporin A and gamma interferon on cultured human keratinocytes. Am J Pathol 131:12-18, 1987.
10. Fisher GJ, Voorhees JJ: Protein kinase C in normal and psoriatic adult human epidermis. Adv Prostaglandin Thromboxane Leukot Res 17B:643-646, 1987.
11. Fisher GJ, Kelley LK, Smith CH: ATP-dependent calcium transport across basal plasma membranes of human placental trophoblast. Am J Physiol 252:38-46, 1987.
12. Fisher GJ, Harris VA, Voorhees JJ: Purification and characterization of calcium/phospholipid-dependent protein kinase from human epidermis. J Invest Dermatol 89:484-488, 1987.
13. Nickoloff BJ, Fisher GJ, Mitra RS, Voorhees JJ: Cytopathic effects of cyclosporine A on human dermal fibroblasts. Transplant Proc 20 (Supl 4) 85-90, 1988.
14. Baldassare JJ, Knipp MA, Henderson PA, Fisher GJ: GTPgS-stimulated hydrolysis of phosphatidylinositol-4,5-bisphosphate by soluble phospholipase C from human platelets requires soluble GTP-binding protein. Biochem Biophys Res Comm 154:351-357, 1988.
15. Elder JT, Gupta AK, Fisher GJ, Voorhees JJ: Cyclosporine inhibits ornithine decarboxylase gene expression and acute inflammation in response to phorbol ester treatment of hairless mouse skin. Transplant Proc 20:95-104, 1988.
16. Gupta AK, Fisher GJ, Elder JT, Nickoloff BJ, Voorhees JJ: Sphingosine inhibits phorbol ester-induced inflammation, ornithine decarboxylase activity and activation of protein kinase C in mouse skin. J Invest Dermatol 91:486-491, 1988.
17. Fisher GJ, Duell EA, Nickoloff BJ, Annesley TM, Kowalke JK, Ellis CN, Voorhees JJ: Levels of cyclosporin in epidermis of treated psoriasis patients differentially inhibit growth of keratinocytes cultured in serum free versus serum containing media. J Invest Dermatol 91:142-146, 1988.

18. Baldassare JJ, Henderson PA, Fisher GJ: Isolation and characterization of one soluble and two membrane-association forms of phosphoinositide-specific phospholipase C from human platelets. Biochemistry 28(14):6010-6016, 1988.

19. Baldassare JJ, Henderson PA, Fisher GJ: Plasma membrane associated phospholipase C from human platelets: synergistic stimulation of phosphatidylinositol-4,5-bisphosphate hydrolysis by thrombin and GTPgS. Biochemistry 28(1):56-60,1989.

20. Elder JT, Fisher GJ, Lindquist PB, Bennett GL, Derynck R, Pittelkow MR, Coffey RJ, Ellingsworth L, Voorhees JJ: Overexpression of transforming growth factor-a in psoriasis. Science 243:811-814, 1989.

21. Takematsu H, Fisher GJ, Voorhees JJ: A novel histone stimulated protein kinase in normal and psoriatic epidermis. J Invest Dermatol 92:385-390, 1989.

22. Pike MC, Lee CS, Elder JT, Voorhees JJ, Fisher GJ: Increased phosphatidylinositol kinase activity in psoriatic epidermis. J Invest Dermatol 92:791-797, 1989.

23. Talwar HS, Fisher GJ, Harris VA, Voorhees JJ: Agonist-induced hydrolysis of phosphoinositides and formation of 1,2-diacylglycerol in adult human keratinocytes. J Invest Dermatol 92:241-245, 1989.

24. Gupta AK, Fisher GJ, Elder JT, Talwar HS, Esmann J, Duell EA, Nickoloff BJ, Voorhees JJ: Topical cyclosporine A inhibits the phorbol ester induced hyperplastic inflammatory response but not protein kinase C activation in mouse epidermis. J Invest Dermatol 93:379-386, 1989.

25. Dyrink R, Lindquist PB, Bringman TS, Wilcox JN, Elder JT, Fisher GJ, Voorhees JJ, Moses HL, Pittelkow M, Coffey RJ: Expression of the transforming growth factor-a gene in tumor cells and normal cells. Cold Spring Harbour Symposium, Cancer Cells, Volume 7, 1989.

26. Fisher GJ, Baldassare JJ, Voorhees JJ: GTP-dependent hydrolysis of phosphatidylinositol-4,5-bisphosphate by soluble phospholipase C from adult human epidermis. J Invest Dermatol 92:831-836, 1989.

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